



# REVISTA BRASILEIRA DE ANESTESIOLOGIA

Publicação Oficial da Sociedade Brasileira de Anestesiologia  
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## REVIEW ARTICLE

# Pain after sternotomy – review



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Received 21 February 2014; accepted 10 September 2014

Available online 23 April 2016

## KEYWORDS

Pain;  
Sternotomy;  
Postoperative  
analgesia

## Abstract

**Background and objective:** Adequate analgesia after sternotomy reduces postoperative adverse events. There are various methods of treating pain after heart surgery, such as infiltration with a local anesthetic, nerve block, opioids, non-steroidal anti-inflammatory drugs, alpha-adrenergic agents, intrathecal and epidural techniques, and multimodal analgesia.

**Content:** A review of the epidemiology, pathophysiology, prevention and treatment of pain after sternotomy. We also discuss the various analgesic therapeutic modalities, emphasizing advantages and disadvantages of each technique.

**Conclusions:** Heart surgery is performed mainly via medium sternotomy, which results in significant postoperative pain and a non-negligible incidence of chronic pain. Effective pain control improves patient satisfaction and clinical outcomes. There is no clearly superior technique. It is believed that a combined multimodal analgesic regimen (using different techniques) is the best approach for treating postoperative pain, maximizing analgesia and reducing side effects.

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## PALAVRAS-CHAVE

Dor;  
Esternotomia;  
Analgesia  
pós-operatória

## Dor após esternotomia – revisão

## Resumo

**Justificativa e objetivo:** Analgesia adequada após esternotomia reduz eventos adversos no pós-operatório. Várias modalidades estão disponíveis para tratamento da dor após cirurgia cardíaca: infiltração com anestésico local, bloqueio de nervos, opioides, anti-inflamatórios não esteroidais, agentes alfa-adrenérgicos, técnicas intratecais e epidurais e analgesia multimodal.

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**Conteúdo:** Foi feita uma revisão sobre epidemiologia, fisiopatologia, prevenção e tratamento da dor após esternotomia. Também foram discutidas as diversas modalidades terapêuticas analgésicas, com ênfase em vantagens e desvantagens de cada técnica.

**Conclusões:** A cirurgia cardíaca é feita principalmente por esternotomia média, que resulta em dor significativa no pós-operatório e uma incidência não insignificante de dor crônica. O controle efetivo da dor melhora a satisfação dos pacientes e os desfechos clínicos. Nenhuma técnica é claramente superior. Acredita-se que um regime analgésico combinado multimodal (com várias técnicas) seja a melhor abordagem para tratar a dor pós-operatória, o que maximiza a analgesia e reduz os efeitos colaterais.

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## Introduction

Due to the large number of cardiac surgeries annually performed and correlation between adequate control of postoperative pain and improved clinical outcomes, anesthesiologists must defend and improve the various current analgesic techniques.<sup>1</sup>

Poststernotomy pain is a complication of cardiac surgery. The incidence, characteristics, and clinical course of pain are not well understood. It is important to determine the incidence and nature of poststernotomy pain for prevention and treatment of pain syndrome.<sup>2</sup>

Poorly controlled pain is associated with sympathetic nervous system activation and increased hormonal response to stress. This response may contribute to the multiple postoperative adverse events, including myocardial ischemia, cardiac arrhythmias, hypercoagulability, pulmonary complications, and increased rates of delirium and wound infection.<sup>3–6</sup> Furthermore, severe pain reduces patient satisfaction, delays the onset of walking, and is associated with the development of postoperative chronic pain.<sup>7</sup>

Inadequate sputum, atelectasis, and pneumonia also occur due to pain. Immobilization by pain causes deep venous thrombosis, which in turn may result in pulmonary thromboembolism. Pain is also a stress factor and causes myocardial infarction, insomnia, and demoralization.<sup>8</sup>

Pain can be classified as acute or chronic, somatic or visceral, and nociceptive or neuropathic. It occurs when tissue injury activates the pain receptors (nociceptors) located in peripheral nerves. During surgery, several procedures can cause tissue trauma, such as incision, coagulation, stretching or shrinkage. There is production and release of substances including prostaglandins and bradykinin, which are pain mediators.<sup>9</sup>

Pain may be associated with many surgical interventions, including incision, saphenous vein removal, pericardiotomy or chest tube insertion, intraoperative dissection and retraction of tissue, among others.<sup>10</sup>

The evaluation and qualification of acute pain can be very variable and depend on the interval between assessments, as well as the instrument used to quantify. Several scales are

used in clinical practice to measure pain, including numeric scale, visual analog, verbal, and facial expression, among others. Some scales are more suitable than others for particular patient populations. The facial expression scale can be used both for patients unable to communicate verbally and patients with tracheostomy.<sup>1</sup>

## Epidemiology

Postoperative pain treatment is important because it is an unavoidable problem involving about 80% of patients undergoing any surgery. Pain is subjective and perceived differently by each patient. However, an inadequate control of pain is common due to fear of side effects of analgesics, both among surgeons and patients.<sup>10</sup>

Despite widely publicized, postoperative pain remains underestimated. Several studies have shown that despite the best treatment results, many patients still suffer from moderate to severe postoperative pain.<sup>11,12</sup>

In a study assessing the intensity of expected pain after most surgical procedures and identifying the procedures in which the current pain therapy is insufficient, 115,775 patients were evaluated in 578 surgical centers. On the first postoperative day, the patients were asked about the most severe pain since surgery, through a verbal numeric scale (0–10). The authors concluded that the 40 procedures with the highest pain scores (mean of 6–7) included 22 orthopedic surgeries or limb trauma. Patients reported high pain scores after minor surgeries, including appendectomy, cholecystectomy, hemorrhoidectomy, and tonsillectomy, while other major surgeries, such as abdominal, resulted in lower pain scores, often due to adequate epidural analgesia.<sup>13</sup>

Studies have described the incidence, severity and risk factors for poststernotomy acute pain. In a study of patients undergoing coronary artery bypass graft, patients were evaluated for four days after surgery. The patients reported more pain than expected: 49% reported severe pain at rest, 78% complained of severe pain when coughing and 62% during movement.<sup>14</sup>

Younger patients seem to be more at risk of developing chronic pain.<sup>15</sup> Patients younger than 60 years had more severe pain than older patients in the early postoperative period after cardiac surgery.<sup>16</sup>

The site of internal mammary artery dissection appears to increase the incidence of postoperative chronic pain.<sup>17</sup> Myofascial syndrome is also common after sternotomy and may contribute to chronic pain. In a review of 1226 patients undergoing sternotomy, the incidence of myofascial syndrome was 15.8%, but in patients with dissected internal mammary artery, the rate was 75.5%.<sup>18</sup>

In another prospective study of 705 patients undergoing cardiac surgery, pain related to the activities was assessed daily until the sixth postoperative day. The patients reported the most severe pain when coughing, after movements, turning around or getting up from bed, and during deep breathing. Although pain scores were high in the immediate postoperative period, patients reported a mean pain score of 4.33 when coughing and of 3.09 during deep breathing on the sixth day after surgery.<sup>19</sup>

In one study, the early removal of chest drains in the first postoperative day, compared to the third day, also reduced pain severity. With the early removal, patients had less pain in the epigastrium, chest, and shoulder on the third postoperative day, without adverse event.<sup>20</sup>

Another factor that reduced surgical pain severity after sternotomy is the pleura preservation, which also improved pulmonary function after surgery.<sup>21</sup>

## Chronic pain

The importance of pain in the early postoperative period as a chronic pain predictor after sternotomy is still uncertain. It was suggested that the severity of postoperative acute pain and the need for large amounts of analgesics during the first postoperative days may be predictive of chronic pain. Thus, it is important to treat the postoperative acute pain in order to stop the possible central and peripheral neural mechanisms responsible for the transition from acute to chronic pain.<sup>2</sup>

The authors of a study evaluated chronic pain in two groups of patients after sternotomy. Patients with myasthenia gravis undergoing thymectomy and those with mammary graft answered questionnaires. There was no difference in postoperative pain duration. Chronic pain was localized, mainly at the site of sternotomy after thymectomy; while after coronary artery bypass graft, it was also located in the upper and lower limbs.<sup>15</sup> Brachial plexus neuropathy was attributed to the fractured fragments of ribs, internal mammary artery dissection, patient positioning during surgery, and central venous catheter place of insertion.<sup>22</sup> Neuralgia of the saphenous nerve was reported after resection of saphenous vein for coronary artery bypass grafting.<sup>23</sup>

In a prospective study, the incidence of chronic pain was evaluated in patients undergoing sternotomy for cardiac surgery. A group of 349 patients was assessed one year after surgery. Of the 318 patients who answered the questionnaire, 28% reported a chest discomfort different from the one prior to surgery. In 13%, the visual analog scale maximum score was 30 mm (moderate pain) and in 4%, it was

54 mm (severe pain). The most common descriptions of the group for pain were: painful prick, penetrating, and burning. The authors concluded that, although the number of patients with poststernotomy pain is high (28%), only a small portion referred severe pain after sternotomy.<sup>2</sup>

Chronic pain after heart surgery may become problematic.<sup>15,24</sup> The cause of persistent pain after sternotomy is multifactorial and includes tissue destruction, intercostal nerve trauma, scar formation, rib fractures, sternal infection, stainless steel sutures and/or costochondral avulsion. Such pain is often located in the arms, shoulders or legs.<sup>25</sup>

In a study of 244 patients after cardiac surgery by sternotomy, persistent pain (defined as pain persisting for more than two months after surgery) was seen in almost 30% of patients.<sup>24</sup> The incidence of persistent pain anywhere was 29% and for sternotomy it was 25%. Other common sites were shoulders (17.4%), back (15.9%), and neck (5.8%). However, this pain was commonly described as average pain, only 7% of patients reported interference with daily activities. The most common words used to describe the pain were annoying (57%), uncomfortable (33%), boring (30%), penetrating (25%), stressful (22%), sensitive (22%), and gripping (22%). The temporal nature was mostly reported as brief/transient and periodic/intermittent. Twenty patients (8%) also reported symptoms of numbness, burning pain, tenderness over the saphenous harvesting site, and symptoms suggestive of acute coronary syndrome. Thus, they concluded that moderate pain after cardiac surgery and sternotomy is common, although it only rarely substantially interfere with daily activities.<sup>24</sup>

## Pathophysiology of acute pain

Postoperative pain mechanisms are complex, but generally speaking, in addition to the nociceptive stimulus from direct tissue trauma, an inflammatory response leads to peripheral and central sensitization in pain experience. Most of the pain after sternotomy occurs because of tissue damage in the skin, subcutaneous tissue, bone, and cartilage.<sup>1</sup>

The intercostal nerves that arise from the thoracic nerve roots innervate the sternum, ribs, and the adjacent subcutaneous tissue. The main thoracic nerves that supply the sternum range from T2 to T6. The parietal pleura is also densely innervated by pain fibers that can be activated by both mechanical and chemical stimulation. In contrast, visceral pleura has no significant sensory innervation. Pericardium is innervated by sensory fibers from the vagus and phrenic nerves and sympathetic trunk.<sup>1</sup>

Several inflammatory mediators are released following tissue injury in surgery, including ions (sodium, potassium and calcium), bradykinin, substance P, histamine, adenosine triphosphate, nitric oxide, prostanooids, and leukotrienes. Some of these molecules directly activate nociceptors, whereas others work by indirect mechanisms. These inflammatory molecules play an important role in the central and peripheral neuronal sensitization before subsequent stimulus.<sup>1</sup>

### Pain treatment

It is usually difficult to achieve satisfactory pain relief after cardiac surgery. Inadequate analgesia or stress response not inhibited during the postoperative period may increase morbidity by hemodynamic, metabolic, immunological, and hemostatic changes.<sup>1</sup>

Pain is subjective and perceived differently by each patient. Inadequate pain control is common due to fear of side effects of analgesics, both among surgeons and patients.<sup>10</sup>

Traditionally, analgesia after heart surgery can be obtained with the use of intravenous opioids (particularly morphine). However, they are associated with harmful adverse events (nausea, vomiting, pruritus, urinary retention, and respiratory depression). Furthermore, long-acting opioids such as morphine may delay postoperative tracheal extubation due to excessive sedation and/or respiratory depression.<sup>25</sup>

For early extubation, anesthesiologists are exploring other options besides the traditional intravenous opioids to control postoperative pain. No technique is clearly superior; probably, a multimodal approach with a combination of analgesics and techniques is the best method to control postoperative pain, maximize analgesia, and minimize adverse events.<sup>25</sup>

### Opioids

Intravenous opioids have been administered to patients undergoing cardiac surgery. Analgesia is reliable and can be used for long period. Disadvantages include pruritus, nausea and vomiting, urinary retention, and respiratory depression.<sup>26</sup>

Intravenous patient-controlled analgesia (PCA) has been used extensively and is a safe and effective method for postoperative pain management.<sup>27,28</sup> PCA was superior to nurse-controlled analgesia in poststernotomy patients.<sup>29</sup>

In a small randomized study, 50 patients received morphine, fentanyl, meperidine, remifentanyl or tramadol with no differences in pain scores, except for patients receiving tramadol who had higher pain scores.<sup>30</sup>

The authors of another study of intravenous PCA with remifentanyl, morphine or fentanyl reported no differences in pain scores. However, patients who received morphine had a higher incidence of nausea and vomiting, while the fentanyl group had more pruritus.<sup>31</sup>

In a study of 60 patients receiving intravenous morphine for pain control after sternotomy, pain scores were lower in patients who received the combination with bolus infusion than those treated with bolus alone; there was no difference in sedation scores and there were no episodes of hypoxia.<sup>32</sup> Also, there was no difference in pain scores or adverse events in another similar study of 100 patients, with intravenous morphine infusion associated with bolus or bolus alone.<sup>33</sup>

Opioids are also involved in a variety of physiological functions, including pituitary management and activity and release of adrenal medulla hormone; cardiovascular and gastrointestinal function management; and breath, mood, appetite, thirst, cell growth, and the immune system

regulation.<sup>34</sup> Opioids may cause various adverse events including respiratory depression, pruritus, nausea and vomiting, urinary retention, constipation, bronchospasm, and hypotension, among others. The potential and well known adverse effects of opioids can limit postoperative recovery.<sup>1</sup>

In summary, opioids are more effective for treating pain after cardiac surgery, particularly when administered by PCA. It seems that there are no clinically significant differences between opioids, and current evidence does not support the use of baseline infusion associated with bolus. Adverse events should be considered when choosing a drug, but if several drugs are appropriate, the cost should be considered.<sup>1</sup> Patients' clinical changes should be considered when selecting a drug.

### Anti-inflammatory drugs

Anti-inflammatory drugs are the most commonly used drugs for postoperative pain treatment. In cardiac surgery, concern about adverse events, such as changes in the gastric mucosal barrier, renal tubular function, and inhibition of platelet aggregation, limits the use of these analgesics. In a study, indomethacin promoted reduction in morphine consumption by PCA and pain scores in the immediate postoperative period of cardiac surgery. There were no differences with patients receiving placebo regarding tracheal extubation time or postoperative blood loss. The authors concluded that the combination of indomethacin suppositories with morphine after cardiac surgery results in a reduction of pain scores and opioid consumption without increasing adverse events.<sup>35</sup> In another study, the use of diclofenac reduced morphine consumption for analgesia after coronary artery bypass graft, via sternotomy, and the same did not occur with ketoprofen or indomethacin versus placebo.<sup>36</sup>

However, other authors obtained no benefit with anti-inflammatory drugs or with paracetamol in patients undergoing cardiac surgery.<sup>36,37</sup>

Proparacetamol, a prodrug of acetaminophen, did not promote reduction in pain scores, oxycodone consumption, and patient satisfaction for analgesia after coronary artery bypass graft via sternotomy.<sup>37</sup>

Etodolac and diclofenac provided slightly better postoperative analgesia (assessed by the analgesic visual scale scores and morphine consumption), and with fewer adverse effects (assessed by antiemetic therapy) than tramadol for postoperative analgesia.<sup>38</sup>

### Infiltration with local anesthetic

The pain after cardiac surgery is generally related to sternotomy, peaking during the first two days after the operation. Due to adverse events associated with intravenous infusion of opioids and anti-inflammatory drugs (gastrointestinal bleeding and renal dysfunction), optional methods for postoperative analgesia were thought.<sup>25</sup>

The postoperative pain treatment with continuous infusion of local anesthetic in the surgical wound was described



after several surgeries in addition to heart surgery.<sup>39</sup> In 36 patients undergoing cardiac surgery, two catheters were placed (one in the subfascial plane above the sternum and the other above the fascia under the skin) in the sternotomy incision at the end of surgery. Patients received 0.25% bupivacaine, 0.5% bupivacaine or saline solution by continuous infusion ( $4\text{ mL h}^{-1}$ ) for 48 h after surgery. There was no difference in extubation time. There was better pain control and lower morphine consumption by PCA postoperatively with 0.5% bupivacaine. The authors concluded that continuous infusion of 0.5% bupivacaine ( $4\text{ mL h}^{-1}$ ) is effective to reduce postoperative pain severity and need for supplementation with opioids, as well as to improve patient satisfaction (early ambulation and reduced hospital stay) after cardiac surgery.<sup>40</sup>

## Nerve block

There has been increased use of nerve block to treat postoperative pain due to the rise in popularity of minimally invasive cardiac surgeries, via minithoracotomy.<sup>41,42</sup>

## Spinal analgesia

The techniques with opioids and/or local anesthetics provide reliable postoperative analgesia in patients after cardiac surgery.<sup>43</sup>

The physicochemical properties of an opioid determine its onset of action, duration, and power via subarachnoid route.<sup>1</sup>

Epidural and subarachnoid anesthesia and analgesia (with local anesthetics or opioids) can inhibit the stress response associated with surgical procedures. Another advantage in cardiac surgery is the heart and thoracic sympathectomy.<sup>44</sup>

Subarachnoid morphine has been used as an adjunct to general anesthesia in cardiac surgery, with better control of postoperative pain and reducing venous opioid requirements.<sup>1</sup> General anesthesia associated with subarachnoid morphine and clonidine reduced pain scores and improved quality of life indicators.<sup>45</sup> Subarachnoid morphine improved pain control and pulmonary function tests, but there was no difference in extubation time.<sup>46</sup> Subarachnoid morphine facilitated tracheal extubation and provided reliable postoperative analgesia.<sup>47</sup> Subarachnoid morphine provided significant analgesia postoperatively.<sup>48</sup> Subarachnoid morphine associated with general anesthesia reduced pain scores, decreased opioid consumption, and improved pulmonary function tests, in addition to minimizing respiratory depression.<sup>49</sup> In other studies, the authors concluded that there was no benefit with the use of subarachnoid morphine.<sup>50</sup>

Subarachnoid bupivacaine attenuated stress response.<sup>51</sup>

Epidural administration of fentanyl and bupivacaine provided reliable analgesia after cardiac surgery.<sup>52</sup> There was no increased risk of hematoma following administration of bupivacaine or ropivacaine (bolus plus infusion) for epidural anesthesia in cardiac surgery.<sup>53</sup> With bupivacaine and fentanyl up to the third postoperative day, there was a reduction in ICU length of stay, early extubation, lower pain

scores, and better results in pulmonary function tests and  $\text{PaO}_2/\text{FiO}_2$  ratio.<sup>54,55</sup>

## Conclusions

Good quality postoperative analgesia is important because it can prevent hemodynamic, metabolic, immunological and hemostatic changes, all of which have the potential to increase postoperative morbidity.

Patient education and the establishment of protocols for pain management are essential.

A large number of approaches can be used to treat acute pain after the surgery, including epidural or subarachnoid, paravertebral and intercostal blocks, intravenous opioids via PCA and adjuvants. However, systemic venous opioids are the mainstay of pain treatment after cardiac surgery. As a general rule, the use of a single type of therapy to treat postoperative pain should be avoided.

## Conflicts of interest

The authors declare no conflicts of interest.

## References

1. Mazzeffi M, Khelemsky Y. Poststernotomy pain: a clinical review. *J Cardiothorac Vasc Anesth*. 2011;25:1163–78.
2. Meyerson J, Thelin S, Gordh T, et al. The incidence of chronic post-sternotomy pain after cardiac surgery – a prospective study. *Acta Anaesthesiol Scand*. 2001;45:940–4.
3. Liu SS, Wu CL. Effect of postoperative analgesia on major postoperative complications: a systematic update of the evidence. *Anesth Analg*. 2007;104:689–702.
4. Popping DM, Elia N, Marret E, et al. Protective effects of epidural analgesia on pulmonary complications after abdominal and thoracic surgery: a meta-analysis. *Arch Surg*. 2008;143:990–9.
5. Singh N, Sidawy AN, Deeze K, et al. The effects of the type of anesthesia on outcomes of lower extremity infrainguinal bypass. *J Vasc Surg*. 2006;44:964–8.
6. Beatties WS, Badner NH, Choi PT. Meta-analysis demonstrates statistically significant reduction in postoperative myocardial infarction with the use of thoracic epidural analgesia. *Anesth Analg*. 2003;97:919–20.
7. Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. *Lancet*. 2006;367:1618–25.
8. Moon MH, Kang JK, Kim HW, et al. Pain after median sternotomy: collateral damage or mitigatable byproduct? *Thorac Cardiovasc Surg*. 2013;61:194–201.
9. Weissman C. The metabolic response to stress: an overview and update. *Anesthesiology*. 1990;73:308.
10. Apfelbaum JL, Chen C, Mehta SS, et al. Postoperative pain experience: results from a national survey suggest postoperative pain continues to be undermanaged. *Anesth Analg*. 2003;97:534–40.
11. Fletcher D, Fermanian C, Mardaye A, et al. Pain and Regional Anesthesia Committee of the French Anesthesia and Intensive Care Society (SFAR): a patient-based national survey on postoperative pain management in France reveals significant achievements and persistent challenges. *Pain*. 2008;137:441–51.

12. Maier C, Nestler N, Richter H, et al. The quality of pain management in German hospitals. *Dtsch Arztebl Int.* 2010;107:607–14.
13. Gerbershagen HJ, Aduckathil S, Van Wijck AJM, et al. Pain intensity on the first day after surgery. *Anesthesiology.* 2013;118:934–44.
14. Lahtinen P, Kokki H, Hynynen M. Pain after cardiac surgery: prospective cohort study of 1-year incidence and intensity. *Anesthesiology.* 2006;105:794–800.
15. Kalso E, Mennander S, Tasmuth T, et al. Chronic post-sternotomy pain. *Acta Anaesthesiol Scand.* 2001;45:935–9.
16. Mueller XM, Tinguely F, Tevaearai HT, et al. Pain location, distribution, and intensity after cardiac surgery. *Chest.* 2000;118:391–6.
17. Mailis A, Umana M, Feindel CM. Anterior intercostal nerve damage after coronary artery bypass graft surgery with use of internal thoracic artery graft. *Ann Thorac Surg.* 2000;69:1455–8.
18. Luleci N, Dere K, Akbas M, et al. Myofascial pain in post-sternotomy patients after cardiac surgery: a clinical study of 1226 patients. *J Back Musculoskelet Rehabil.* 2008;21:239–43.
19. Milgrom LB, Brooks JA, Qi R. Pain levels experienced with activities after cardiac surgery. *Am J Crit Care.* 2004;13:116–25.
20. Mueller XM, Tinguely F, Tevaearai HT, et al. Impact of chest tube drainage on pain after cardiac surgery. *Eur J Cardiothorac Surg.* 2000;18:570–4.
21. Gullu AU, Ekinci A, Sensoz Y, et al. Preserved pleural integrity provides better respiratory function and pain score after coronary surgery. *J Cardiovasc Surg.* 2009;24:374–8.
22. Sharma AD, Parmley CL, Sreeram G, et al. Peripheral nerve injuries during cardiac surgery: risk factors, diagnosis, prognosis, and prevention. *Anesth Analg.* 1989;69:81–2.
23. Mountney J, Wilkinson GAL. Saphenous neuralgia after coronary artery bypass grafting. *Eur J Cardiothorac Surg.* 1999;16:440–3.
24. Ho SC, Royse CF, Royse AG, et al. Persistent pain after cardiac surgery: an audit of high thoracic epidural and primary opioid analgesia therapies. *Anesth Analg.* 2002;95:820.
25. Myles PS, Daly DJ, Djaiani G, et al. A systematic review of the safety and effectiveness of fast-track cardiac anesthesia. *Anesthesiology.* 2003;99:982.
26. Raja SN, Lowenstein E. The birth of opioid anesthesia. *Anesthesiology.* 2004;100:1013–5.
27. Macintyre PE. Safety and efficacy of patient-controlled analgesia. *Br J Anaesth.* 2001;87:36–46.
28. Walder B, Schafer M, Henzi I. Efficacy and safety of patient controlled opioid analgesia for acute post-operative pain. A quantitative systematic review. *Acta Anaesthesiol Scand.* 2001;45:795–804.
29. Pettersson PH, Lindskog A, Owall A. A patient-controlled versus nurse-controlled pain treatment after coronary artery bypass grafting. *Acta Anaesthesiol Scand.* 2000;44:43–7.
30. Oztekin DS, Oztekin I, Issever H. Postoperative effects of opioid analgesics administered via continuous perfusion and patient controlled analgesia after open heart surgery. *Yakugaku Zasshi.* 2006;26:499–504.
31. Gurbet A, Goren S, Sahin S, et al. Comparison of analgesic effects of morphine, fentanyl, and remifentanyl with intravenous patient controlled analgesia after cardiac surgery. *J Cardiothorac Vasc Anesth.* 2004;18:755–8.
32. Guler T, Unlugenc H, Gundogan Z. A background infusion of morphine enhances patient-controlled analgesia after cardiac surgery. *Can J Anaesth.* 2004;51:718–22.
33. Mota FA, Marcolan JF, Pereira MH, et al. Comparison study of two different patient-controlled anesthesia regimens after cardiac surgery. *Rev Bras Cir Cardiovasc.* 2010;25:38–44.
34. Kehlet H, Rung GW, Callesen T. Postoperative opioid analgesia: time for reconsideration? *J Clin Anesth.* 1996;8:441.
35. Rapanos T, Murphy P, Szalai JP. Rectal indomethacin reduces postoperative pain and morphine use after cardiac surgery. *Can J Anesth.* 1999;46:725.
36. Hynninen MS, Cheng DCH, Hossain I. Non-steroidal antiinflammatory drugs in treatment of postoperative pain after cardiac surgery. *Can J Anesth.* 2000;47:1182.
37. Lahtinen P, Kokki H, Hendolin H. Propacetamol as adjunctive treatment for postoperative pain after cardiac surgery. *Anesth Analg.* 2002;95:813.
38. Immer FF, Immer-Bansi AS, Trachsel N. Pain treatment with a COX-2 inhibitor after coronary artery bypass operation: a randomized trial. *Ann Thorac Surg.* 2003;75:490.
39. Brown SL, Morrison AE. Local anesthetic infusion pump systems adverse events reported to the Food and Drug Administration. *Anesthesiology.* 2004;100:1305.
40. White PF, Rawal S, Latham P, et al. Use of a continuous local anesthetic infusion for pain management after median sternotomy. *Anesthesiology.* 2003;99:918–23.
41. Soto RG, Fu ES. Acute pain management for patients undergoing thoracotomy. *Ann Thorac Surg.* 2003;75:1349.
42. Bilgin M, Akcali Y, Oguzkaya F. Extrapleural regional versus systemic analgesia for relieving postthoracotomy pain: a clinical study of bupivacaine compared with metamizol. *J Thorac Cardiovasc Surg.* 2003;126:1580.
43. Chaney MA. Intrathecal and epidural anesthesia and analgesia for cardiac surgery. *Anesth Analg.* 1997;84:1211.
44. Liu S, Carpenter RL, Neal MJ. Epidural anesthesia and analgesia: their role in postoperative outcome. *Anesthesiology.* 1995;82:1474.
45. Lena P, Balarac N, Lena D, et al. Fast-track anesthesia with remifentanyl and spinal analgesia for cardiac surgery: the effect on pain control and quality of recovery. *J Cardiothorac Vasc Anesth.* 2008;22:536–42.
46. Jacobsohn E, Lee TWR, Amadeo RJ, et al. Low-dose intrathecal morphine does not delay early extubation after cardiac surgery. *Can J Anaesth.* 2005;52:848–57.
47. Bettex DA, Schmidlin D, Chassot PG, et al. Intrathecal sufentanil-morphine shortens the duration of intubation and improves analgesia in fast-track cardiac surgery. *Can J Anesth.* 2002;49:711.
48. Alhashemi JA, Sharpe MD, Harris CL, et al. Effect of sub-arachnoid morphine administration on extubation time after coronary artery bypass graft surgery. *J Cardiothorac Vasc Anesth.* 2000;14:639.
49. Fitzpatrick GJ, Moriarty DC. Moriarty: intrathecal morphine in the management of pain following cardiac surgery. A comparison with IV morphine. *Br J Anaesth.* 1988;60:639–44.
50. Latham P, Zarate E, White PF, et al. Fast-track cardiac anesthesia: a comparison of remifentanyl plus intrathecal morphine with sufentanil in a desflurane-based anesthetic. *J Cardiothorac Vasc Anesth.* 2000;14:645–51.
51. Lee TW, Grocott HP, Schwinn D, et al. High spinal anesthesia for cardiac surgery: effects on alpha-adrenergic receptor function, stress response, and hemodynamics. *Anesthesiology.* 2003;98:499.
52. Royse C, Royse A, Soeding P. Prospective randomized trial of high thoracic epidural analgesia for coronary artery bypass surgery. *Ann Thorac Surg.* 2003;75:93.

53. Pastor MC, Sanchez MJ, Casas M. Thoracic epidural analgesia in coronary artery bypass graft surgery: seven years' experience. *J Cardiothorac Vasc Anesth.* 2003;17:154.
54. Sharma M, Mehta Y, Sawhney R, et al. Thoracic epidural analgesia in obese patients with body mass index of more than 30 kg/m<sup>2</sup> for off pump coronary artery bypass surgery. *Ann Card Anaesth.* 2010;13:28–33.
55. Mehta Y, Vats M, Sharma M, et al. Thoracic epidural analgesia for off-pump coronary artery bypass surgery in patients with chronic obstructive pulmonary disease. *Ann Card Anaesth.* 2010;13:224–30.